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REVIEW ARTICLE

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Why we should be avoiding periorificial mimetic muscles when injecting tissue fillers

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Abstract

Background: Tissue fillers are generally safe and well tolerated by patients. However, complications do occur and may be very severe, such as intravascular injection (with occasional residual tissue loss, visual and neurological sequelae) and late nodularity and swelling. Methods to lessen the likelihood of complications have been the subject of much recent literature. Depth of injection has been identified as a key safety consideration.

Patients/Methods: The role of injection of facial filler into the muscular layer of the face is explored in this article. Literature was explored using available search facilities to study the role of injections in or around this layer in the production of significant adverse reactions.

Results: A body of literature seems to suggest that injection into mimetic musculature of the face especially the musculature in the periorbital and perioral regions is prone to adverse reactions.

Conclusions: Injection of agents into the perioral and periorbital mimetic muscular layer may produce, product clumping, displacement, and tendency to late nodularity and swelling. It also risks intravascular injection as compared to injection of other layers of the face. Injection into the mimetic muscles especially the sphincteric muscles should be avoided to minimize the risk of complications.

KEYWORDS

COVID-19, mimetic muscles, orbicularis oculi, orbicularis oris, Tissue fillers

1 | INTRODUCTION

The burgeoning use of filling materials has brought with it an increasing interest in safety aspects of these agents. Although well-tolerated in general, there are serious albeit rare adverse reactions that demand attention.

2 | ADVERSE REACTIONS

Adverse reactions to filler materials may be divided into vascular[1,2] and nonvascular issues.[3,4]

The vascular issues have been well-described. They consist of the following:

- Minor bruising and ecchymosis from transient contact with or puncture of the prevailing vasculature
- True intravascular injection and embolization of fillers with tissue ischemia in the angiosome distribution of the vascular occlusion.[5] Dependent on the exact anatomy of the obstruction, tissue loss may be cutaneous only and/or involve deeper structures
- Distant embolization of fillers, in some individuals, may result in partial or complete unilateral and rarely bilateral visual loss and neurological deficit

Nonvascular issues may include:

- Misplacement or over correction often by poor injection technique or product choice
- Inadvertent placement into the retroorbital space
- Migration of a high G prime filler from the cheek into the tear trough region.
- Frank sepsis, which is serious but rare and usually seen in the context of a break in sterile technique or patient-related factors such as poor local barrier function with altered local skin microbiome

Recently, the problem of delayed or late reactions to fillers has been more frequently reported and has been the subject of multiple consensus documents. These reactions include the following:

- Late noninflammatory appearing nodules/swelling- occasionally filler material—especially in the infraorbital zone sometimes many years post filler injection. Many theories have been asserted for this late occurrence, but most rely on the interplay of the orbicularis function and the lack of natural dissolution of product in the periorbital area
- Evanescent and sometimes recurrent noninflammatory and inflammatory reactions appearing at times of heightened immune activity such as viral infections, which are common in both periorbital and perioral regions
- More fixed and problematic noninflammatory and inflammatory reactions which may arise weeks or months post injection. These would appear to be an interplay between the presence and metabolism of the filler, infection, and host inflammation. It is probable that host factors influence all of these with the reaction to infection, extent of the inflammatory reaction and the metabolism of the filler all possibly varying in different individuals

3 | THE PERIORAL AND PERIORBITAL MUSCULATURE

The orbicularis muscles surrounding the eyes and the mouth are similar in many respects. They both function to maintain or coordinate opening and closing functions of the eyes and mouth, and they both contribute to nonverbal communication and age determination, through their insertion into the dermis for expression and wrinkle production. They both fuse and coordinate with surrounding muscles to enable the multiple coordinated actions required for their basic functions as well as their role in expressions in both verbal and nonverbal forms.

They differ in a number of aspects. The orbicularis oculus muscle is more of a true sphincteric muscle.[6] Its functions are to close the eyelid and assist in pumping the tears into the nasolacrimal system. The orbicularis oculus muscle is a large muscle with three components. The outermost is the orbital component under voluntary control to allow expressions such as closing the eye, winking and smiling, the next section moving inward toward the eye is the pre-septal component which functions to squeeze the eyes shut either by voluntary or involuntary blink response means and the innermost pre-tarsal that keeps the eyelids opposed during sleep. The orbital component attaches medially to the medial canthal tendon and periosteum whereas the pre-septal and pre-tarsal components divide medially into deep and superficial heads before insertion. Laterally, the muscle attaches to the lateral canthal tendon, raphe, and surrounding tissues.

The orbicularis oris muscle has no periosteal or bony insertions and is not a true sphincteric muscle being made of four cooperating quadrants. It also has two layers—a deep layer acting as a constrictor cooperating in mastication and the superficial muscle layer related to speech and facial expressions. Much of the attachment of the orbicularis oris is to the modiolus bilaterally and to the muscles of expression for the superficial component.[7]

4 | METHODS

Literature search databases (PubMed, Ovid, and Google Scholar) were examined for articles on mimetic muscles, intramuscular injections and fillers, and filler reactions and combinations and variations of these terms. The anatomy of the periorbital and perioral zones was also searched and explored to assess any unusual aspects of these sphincter muscles that may contribute to adverse issues.

5 | RESULTS

Results from these searches raised some concerns about adverse reactions both by the possibility of intravascular injection and extravascular reactions and repositioning of product relating to injecting filler materials into the mimetic muscles.

6 | DISCUSSION

The issues with the muscular layer and fillers.

6.1 | Vascular issues

These periorificial muscles are dynamic and very active muscles. They have abundant blood supply and important vascular

connections. This is seen by the frequency of bruising on injecting either around the eyes and the mouth. In the perioral area, the large vessels of the inferior and superior labial arteries along with the mental and submental all are potential embolic targets.[8,9] These tend to run either just superior or inferior to the muscles of the perioral region. There is much variability of vascular architecture within the horizontal layer but far less variability in their depth. It is thus advisable to keep away from these structures by gleaning an understanding of vascular anatomy in each area of injection and maintaining a respectful distance from major vessels. However, even depth is imperfect, with variability in the superior labial artery from its usual plane in greater than 20% of cadavers[10] being between the orbicularis muscle and the mucosa in 78%, between the superficial and deep parts of the orbicularis muscle in 17.5% and superficial to the muscle (between the skin and the orbicularis muscle in 2.1%). As the vessels tend to track the muscles rather intimately, keeping clear of these structures would seem prudent. A notable exception to this variation of vascular anatomy and where depth is fixed pertains to the emergence of the supratrochlear, supraorbital, zygomaticofacial, zygomaticotemporal, infraorbital, and mental arteries through their foramina. These regions should be avoided at depth or approached in a fashion to minimize the chance of intravascular injection. Around the eyes, vascular supply emanates from the facial and superficial temporal as well as the ophthalmic arteries.[11] Similarly, it is usually advised around the eyes that deep injection below the muscular layer or superficial injection above it are safer options than intramuscular injections. However, medially in the tear trough, this is not practical as the muscle is tightly bound to the periosteum.[12]

6.2 | Mechanical effects

The periorificial muscles act as squeezing muscles closing their orificial structures. Any material implanted in these structures is likely to be displaced. This may lead to anterior displacement of product in the infraorbital zone if it is placed into the muscles. Added to this, injection even if intended to be deep may in fact be intramuscular in this zone.[13,14] In the perioral zone, constant muscle movement, which cannot be prevented during speech and mastication, can compress an injected linear strand to a lump. Therefore, intramuscular injection may lead to clumping and increase the chance of nodule formation with Poly-L-Lactic Acid. The incidence appears to be reduced when the perioral and periorbital zones are avoided.[15,16] It is suggested by manufacturers of Calcium hydroxyapatite and acrylate fillers that the regions around the eyes and mouth are not targeted.[17,18] It is unknown at this time whether the higher incidence of clumping or nodules with these products is because the intramuscular injection is specifically the risk or the higher movement or metabolic activity of these areas or other the effect of unknown factors. Autologous fat injection into muscles was a technique described close to 20 years ago but has not been described often over recent years.[19,20]

In addition, the muscles of facial expression lack an enveloping fascia, that is, epimysium with the exception of the buccinator muscle. Furthermore, most of the facial muscles change planes from layer 5 to layer 2 in the face.[21] Thus theoretically, the filling substance may not remain contained within the muscle where initially placed but may over time end up in multiple planes or extruded from the muscle.

6.3 | Metabolic effects

The metabolic activity inherent in the musculature and its supporting vasculature may support vigorous inflammatory responses once initiated. A strict sterile, or clean environment, is difficult to maintain in the perioral zone prior to, during, and after procedure, and introduction of bacteria is likely with all injections. It is probable that the periphery of the filler injected is what is subjected initially and over time to degradative forces via specific enzymes such as hyaluronidase and reactive oxygen species via inflammation. The continual mechanical distortion of boluses of material may break down larger clumps of fillers exposing them to more metabolic activity and potential inflammatory effects.

6.4 | Specific use of hyaluronic acid fillers

As most injections in these regions are now hyaluronic acid, it is useful to look at the recent literature in relation to delayed nodules with these agents. Both regions are susceptible to late nodule development with this agent.

The preceding discussion is very pertinent to these agents. It is likely that over time the following may occur. Over the weeks or months after injection, a bolus of hyaluronic acid (HA) filler may be expected to be degraded on the periphery of the bolus by local enzymatic activity and inflammatory mediators. All HA filler materials start as high molecular weight hyaluronic acid compounds (>1000 kDa). Some fillers have lower hyaluronic HA (>500 kDa) in combination with high molecular weight HA but even this is far away from low molecular weight HA (10-250 kDa). Low molecular weight HA (10-20 kDa) is the eventual breakdown product of all HA products, and if this occurs at a normal rate, it will be seen as gradual loss of filler volume over time.

Current observation shows that a bolus of filler if implanted within muscle may follow a different cascade. Over time, the periphery will be exposed to normal metabolic degradation, but mechanical effects may induce change in, or magnification of the filler surface area over time. In one study, 5 of 7 explanted facial implants demonstrated biofilm formation under electron microscopy, and rougher, more porous surfaces displayed more severe biofilm formation than smoother implants. Theoretically, this could be extrapolated to HA filler in the above circumstance.[22,23] In the presence of either implanted bacteria or hematogenous derived pathogens at the periphery of the filler, the resultant inflammation to this infection will cause accelerated degradation of the HA filler to low molecular weight hyaluronic acid. Low molecular

weight HAs are pro-inflammatory and may create a feedback loop inducing further inflammation. A case report describes progressively worsening eyelid edema with histopathological evidence of degenerating striated muscle surrounding pools of hyaluronic acid.[24] Chronic inflammation or toxicity secondary to filler breakdown products were put forward as possible explanations.[25,26] Certain HA agents may be more prone to this activation than others. Certain patients may be able to mount reactions more significantly than other patients and the infective agent will illicit differing effects depending on its relative virulence. Injecting into muscles is likely in both the periorbital and perioral zones to create a suitable environment amplifying the likelihood of this activity.

6.5 | Injecting the perioral and periorbital zones

To decrease the rate of delayed nodules in these areas, it is best to lay down very small aliquots or layers that may be more difficult to clump or alter with mechanical movement. It is advisable to inject slowly to decrease trauma to the tissues and to avoid intravascular injection. It is imperative that sterility is maximized especially in the perioral area. This includes complete face washing and recurrent use of antiseptics locally throughout the injection process. It may be that in the current COVID-19 pandemic that use of mouth, nose, and eye antiviral irrigation may become commonplace. From the foregoing discussion, avoiding the muscular layer is also recommended. All this becomes more important when using certain product lines. HA products are possibly not all the same. Some may have a higher rate of issues than others and many may have a higher rate of issues when introduced to a market than they do after market experience. In jurisdictions where teaching has been to avoid the muscular layer, large boluses and rapid injections the complication rate appears to be less.

6.6 | COVID-19 and periorificial treatment

There is now an additional confounder for injecting in the perioral and periorbital zone, the risk of contamination in a patient carrying or presymptomatic of COVID-19. Although not common, COVID-19 has been found in ocular secretions with reports of ophthalmologists and otolaryngologists dying of coronavirus.[27] The nose and surrounding zones and the mouth and perioral area are more concerning[28] especially as fillers in these areas are so common. Treatment of these areas may be problematic at this time but if they are attempted, decreasing viral load with mouth rinses and nasal applications may be an important consideration.[29]

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